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Keywords: Compromised socket; Cortical lamina; Extraction socket; Porcine bone substitute; Ridge preservation.

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Ridge preservation of compromised extraction sockets applying a soft cortical membrane: A canine proof-of-principle evaluation

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Running head: Socket rebuilding with a soft cortical membrane

Keywords: Extraction socket, ridge preservation, cortical lamina, compromised socket, porcine bone substitute

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Abstract

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xenogenic graft material was undergoing remodelling processes while allowing adequate bone regeneration.

1. Introduction

Maintaining hard and soft tissue architecture after tooth extraction represents a prerequisite to achieve functional and esthetic results. Conventional tooth extraction is still performed without any additional tissue manipulation in routine dental practice. The formed blood clot serves as a natural scaffold for granulation tissue formation and, finally, to new bone formation (Devlin and Sloan, 2002; Kanyama et al., 2003). Soft tissue closure of the extraction site by keratinized tissue is established after about 24-35 days (Amler, 1969). However, interim healing by granulation tissue may result in vertical and horizontal hard and soft tissue volume reduction. Bone loss in horizontal dimension may account for up to 5–7 mm in the first ten months, which corresponds to approximately 50 % of the original width of the alveolar bone (Schropp et al., 2003). It has been shown that particularly the buccal bone plate is resorbed during healing process leading to collapse and shrinkage of surrounding soft tissues as well (Araujo and Lindhe, 2005).

Different treatment options of extraction socket – generally accepted as a standard treatment approach - have therefore been considered and controversially discussed in literature. Several studies have proposed various ridge preservation techniques, including placement of graft materials and/or usage of occlusive membranes focusing on preservation and regeneration of hard tissue (Artzi and Nemcovsky, 1998; Artzi et al., 2000; Cardaropoli et al., 2005; Carmagnola et al., 2003b; Elian et al., 2007; Fickl et al., 2007; Lekovic et al., 1998; Lekovic et al., 1997). As a conclusion, most studies demonstrated that ridge preservation techniques are beneficial in maintaining the hard tissue volume to a certain extent. However, a complete preservation and regeneration of the bone volume after tooth extraction has not been reported, especially in compromised sites with partial or complete loss of the buccal bone plate, nevertheless, these deficient sockets (Carmagnola et al., 2003b; Fickl et al., 2008a; Nevins et al., 2006). There is no evidence to support the superiority of one technique over another. There is also no conclusive evidence that ridge preservation procedures improve the ability to place implants or the long-term outcome of implants (Darby et al., 2009). So far, mainly deproteinized bovine bone was investigated. As a significant shortcoming, incomplete bone regeneration and soft tissue encapsulation was reported (Fickl et al., 2017; Fischer et al., 2018) and clinical relevance of this incomplete regeneration on long-term implant success stays unclear (Thoma et al., 2017). Collagenated porcine bone substitutes are another alternative biomaterial and have been investigated in pre-clinical (Fischer et al., 2015) and clinical studies (Barone et al., 2014a; Barone et al., 2014b; Barone et al., 2015) showing promising results with regard to turnover into new bone while maintaining the ridge dimension. Furthermore, these studies often only evaluate intact extraction sockets, while, under most clinical circumstances, at least parts of the bony housing of the tooth (e.g. buccal wall) is missing or gets lost during socket remodeling. In case of a deficient bone wall, raising a flap and covering the applied biomaterial is mostly needed, resulting in further bone loss (Fickl et al., 2011) and shift of the muco-gingival border. Especially in deficient sockets, however, placing a membrane and/or a soft tissue graft seems to improve the clinical outcome (Jambhekar et al., 2015). Most animal models focus on posterior teeth and results are extrapolated ever since. Today, there is no pre-clinical animal model which allows investigation in anterior teeth, however, anterior teeth are the main target for ridge preservation procedures or immediate implant placement in daily clinical practice.

Therefore, the aim of this proof-of-principle evaluation was to assess the use of a porcine soft cortical membrane in combination with a porcine graft material aiming to restore the original ridge contour and to achieve complete bone regeneration in case of a missing buccal wall without raising a flap and attempting primary wound closure. In this study, osteogenesis of the buccal regions around the membrane and healing of the alveolar socket was the main focus.

2. Material and Methods

All surgeries were performed under the supervision of a veterinary. The Ethics Committee for Animal Research at the University of Budapest approved the study protocol (PEI/001/961-2/2013). One beagle dog was used for this experiment. Clinical examination prior to intervention revealed good general health of the animal including intact jaws without any dental trauma or mucosal lesions.

2.1. Interventions

The animal was pre-anesthetized with intramuscular injection of a mixture of acepromazine 0.25 mg/kg, buprenorphine 0.01 mg/kg, and medetomidine 35 µg/kg. In the surgery theatre, an intravenous catheter was inserted into the cephalic vein, and propofol (0.4 mg/kg/min) was infused. A local anaesthesia (articaine 40 mg, 1% epinephrine) was injected at the respective intraoral sites for additional pain control and blood homeostasis.

To create standardized buccal dehiscences of about 50% of root length, a first surgery was performed to remove the buccal bone at the distal roots of the 3rd and 4th mandibular premolars (Fig. 1). For this purpose, a full-thickness flap was raised and the bone was removed with rotating instruments, chisels and curettes. Afterwards, flaps were readapted to achieve primary wound closure.

One month later, a second surgery was performed (“tooth extraction & ridge preservation”). The 3rd and 4th mandibular premolars were hemisected, the mesial root was endodontically treated and the distal root was extracted without raising a flap.

To allow for placement of the 0.5 mm semi-rigid membrane (Osteobiol Lamina®, Tecnoss, Giaveno, Italy) outside of the extraction socket and therefore recreating the buccal bone wall, a pouch was prepared within the soft tissue using micro-blades and tunnelling knives (Fig. 2). This membrane is made by down-grinding porcine cortical bone and, after superficial decalcification, acquires some flexibility while maintaining the compactness of the original bone structure derived from and a barrier function. Unlike other xenogenic bone substitutes, Lamina® does not get treated with high temperature. After placement of the membrane, the socket was filled with a collagen-modified porcine bone substitute (Osteobiol Gen-Os®, Tecnoss), which was placed to the level of the surrounding bone height (Fig. 3). To support surrounding soft tissues and to close socket orifice, a porcine dermal matrix (Osteobiol Derma®, Tecnoss) was sutured over the socket (Fig. 4).

After surgery, the animal was monitored once per day for any clinical complications or side effects. The dog was placed on soft diet throughout the entire observation period. Tooth cleaning and administration of 0.2 % chlorhexidine solution was performed for four weeks.

2.2. Histologic procedure

Four months after the second surgery, the dog was sacrificed and the extraction sites were dissected in blocks with a diamond saw in a frontal (bucco-lingual) and sagittal orientation. In a first step, radiographs were performed on the retrieved segments in a.-p. direction. Afterwards, samples were fixed in formaldehyde, dehydrated and infiltrated with ultraviolet light-activated polymethylmethacrylate (PMMA, Technovit 72100®, Heraeus Kulzer, Hanau, Germany) for one week. This procedure was followed by a 3-day immersion in a 1:1 combination of PMMA and 2-hydroxyethylmethacrylate (GMA, Heraeus Kulzer). After subsequent immersion in 100% embedding medium, samples were polymerized under high power UV-light in three steps. Parallel sections were then cut from the specimens using a microsaw device (EXAKT Advanced Technologies, Norderstedt, Germany) and grinded up to 20 µm thickness using a microgrinding system (EXAKT). Sections were stained using toluidine blue staining without the removal of the plastic medium. All grinded sections were photographed (1:1) with a reflecting microscope (Leica, Wetzlar, Germany) using a Leica camera DFC420 with software V3.8 (Leica) and evaluated under a light microscope (Zeiss-Axio-Imager®, Zeiss, Jena, Germany) at original magnifications between 5x and 50x. All biopsies were cut and grinded in serial sections and all sections were evaluated.

3. Results

No adverse complications were observed neither intra- nor post-operatively with respect to animal or surgical sites. For instance, no wound dehiscence or abscess was observed.

3.1. Radiological and histological findings

The ground sections were first visualized with radiographs to identify the regions of socket healing after bone substitute application and bone repair. The peri-apical radiographs did not reveal any impaired healing and good maintenance of the bone height. Due to some orientation problems during preparing the sections and due to the small number of sockets, the original aim to volumetrically compare the four augmented sockets with the corresponding retained roots, as described earlier (Fischer et al., 2015), had to be withdrawn.

3.2. Socket healing

In the ground sections of all sites, the area of socket healing could be identified as a radio-dense cylindrical or pyramid-like zone (Fig. 5). At lower magnification, these histological areas could also be identified in mesio-distal serial sections (Fig. 6), again, showing good preservation and regeneration of the sockets compared to the retained roots. At higher magnification, different stages of osteogenesis and bone formation were visible in the augmented areas. The augmented socket consisted of aggregation of bone substitute granules appearing as cortical lamellar bone showing peri-granular osteogenesis presenting with osteoid formation, but also larger areas of newly formed woven bone connecting the granules were visible (Figs. 7a-d). At the border between membrane and augmented areas, ossicles covered by osteoblast seams were also observed. Focally, resorption lacunae were visible on the surfaces of single porcine bone substitute granules indicating the remodelling (Fig. 7d).

3.3. Buccal bone repair

In the buccal-lingual grinding sections, a regeneration of a thin buccal lamella was clearly visible (Figs. 8a, b). Newly formed bone was visible under the soft cortical membrane. At higher magnification, osteogenesis along the membrane could be observed. Bony protrusions and blebs or small ossicles outside the former bone borders were observed (Figs. 8a). The newly formed bone consisted of mostly woven bone and was covered by osteoblasts. Focally, the membrane showed signs of degradation. In some cases, remnants of the membrane were incorporated into the newly formed bone.

4. Discussion

The present proof-of-principle dog evaluation study aimed to evaluate healing of compromised extraction sockets with a partially missing buccal bone wall treated with a soft cortical membrane without raising a flap for primary closure. The following major observations were made: i) regeneration of a deficient socket seems to be possible applying the presented approach enabling implant placement; ii) the soft cortical membrane was sufficiently stable to form and stabilize the bone contour and to inhibit soft tissue invasion, thereby, promoting bone regeneration; iii) the xenogenic bone substitute was undergoing remodelling while allowing bone regeneration within the extraction socket defect. This promising technique might be used in aesthetically challenging situation e.g. immediate buccal bone reconstruction in conjunction with immediate implant placement without the need to raise a flap. The above-mentioned results need to be approved in a clinical setting in anterior extraction sockets.

Several reviews systematically investigated the field of ridge preservation (Darby et al., 2009). Socket preservation techniques conceptually aim to entirely stop volumetric changes after tooth extraction. However, no such technique was described yet, which could completely and predictably achieve this ideal goal. Ridge preservation, hence, should at least help to reduce bone dimensional changes with regard to height and width loss enabling implant placement without further augmentation (Ten Heggeler et al., 2011). Horizontal dimensional reduction seems to be more distinctive than vertical reduction and more loss occurs in the first 3-6 months' post-extraction. Human studies have shown horizontal bone loss of 29-63% and vertical bone loss of 11-22% after six months (Tan et al., 2012). Multiple techniques have been proposed for ridge preservation after tooth extraction mainly using and adapting guided bone regeneration techniques or solely placing a bone material. Comparing different methods applying a bovine bone substitute alone or with a free gingival graft or with a collagen membrane, no approach was found to be able to entirely compensate for the alterations after tooth extraction and in respect of the buccal bone plate as well (Fickl et al., 2008b; Fickl et al., 2008c). Application of a bone substitute only (w/o membrane) seems also not to be able to entirely stop the ridge shrinkage and even might delay healing (Araujo et al., 2009). Furthermore, the bone substitutes might not be well integrated in newly formed bone, but are rather encapsulated in connective tissue, especially in the coronal aspect (Carmagnola et al., 2003a). Application of a barrier membrane seems to improve the results after ridge preservation (Faria-Almeida et al., 2019). The material combination used in this study has been shown to effectively preserve fully intact extraction sockets, however, with the shortcoming of raising a flap for primary closure (Festa et al., 2013). In the present evaluation, we found healing of the extraction socket without any signs of inflammation or foreign body reactions in all analysed sections and, moreover, remodelling of the applied collagenated bone substitute was seen. Similar observations were found in biopsies from humans and rabbits (Kim et al., 2009; Nannmark and Sennerby, 2008; Pagliani et al., 2012; Rossi et al., 2016), where peri- and intergranular osteogenesis with osteoblast seams were observed. No soft tissue encapsulation has been seen as reported for other xenografts (Carmagnola et al., 2003a; Thoma et al., 2017). Even advanced stages of osteogenesis revealing remodelling by osteoclasts was visible. These findings corroborate the osteoconductive functions of the bone substitute material applied in this study. It has been shown that the presence of collagen in this material favours vascular ingrowth during healing (Rombouts et al., 2016). By finding resorption lacunae on the surface of some granules, there are also indications that the material applied shows signs of resorption. Osteogenesis along and near the cortical membrane was also obvious in our histological findings. This indicates osteoconductive properties of this type of membrane as it has already been described after histological analysis of clinical cases of alveolar ridge augmentation (Rossi et al., 2016). Due to the mechanical properties of this membrane it might be superior to traditional collagen membranes in cases with higher demands for defects stabilization. The biggest shortcomings of this study are missing controls and investigation in only one animal. Since no control was applied, we can only extrapolate the true effect of the presented socket grafting technique, meaning, that maybe the sockets would have healed by only using one of the applied biomaterials (bone substitute versus barrier membrane) or even without any intervention in this canine model. It is not clear whether the present defects can be regarded as a chronic defect, nevertheless no spontaneous healing has been observed in a similar model (Fickl et al., 2014). The level of evidence of a pre-clinical model is limited and, since a living animal is sacrificed, only as many animals as needed should be used. This study clearly shows the potential of the approach and might be directly transferred into a clinical study. Additional 3D-imaging might be included in future studies to evaluate the bony defects and repair at different time points. A limitation of this study from a histological point of view is the use of grinding sections which do not allow to identify details of the membrane induced osteogenesis on tissue and cellular level due to the reduced resolution of microscopy.

Hence, within the limitations of this study, the original hypothesis of regeneration of the missing buccal socket wall was approved. Since this study was conducted as a proof-of-principle with only one animal and consequently a limited number of specimens, further research is needed to evaluate the presented approach and material combination clinically and to investigate details of the membrane biology. A randomized controlled clinical study focusing on deficient extraction sockets together with e.g. flapless immediate implant placement or ridge preservation especially in the anterior maxilla are needed at this point.

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interest. The study was funded by the authors institutions and partially by an unrestricted grant from Tecnoss Dental Srl., Turin, Italy, for e.g. travelling costs & biomaterials.

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Legends

Fig. 1: To create standardized buccal dehiscences (6x3 mm), a first surgery was performed to remove the buccal bone at the distal roots of the mandibular premolars.

Fig. 2: A pouch was prepared within the soft tissue on the buccal side to allow for placement of the soft cortical membrane (Osteobiol Lamina®) outside of the extraction socket and therefore recreating the buccal bone wall.

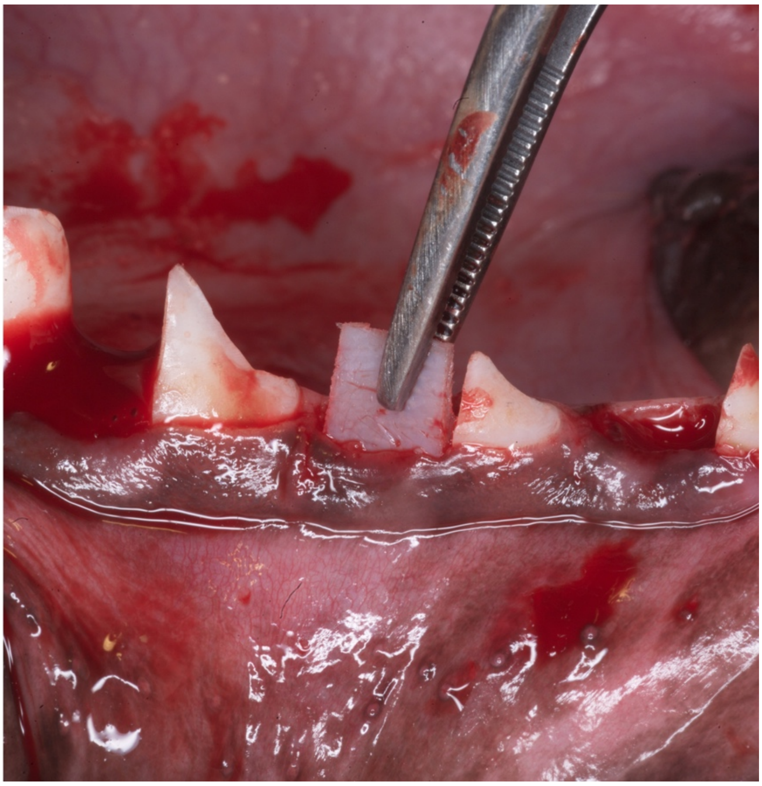


Fig. 3: After placement of the membrane, sockets were filled with a collagenated porcine bone graft material (Osteobiol Gen-Os®) to the level of the surrounding bone height.

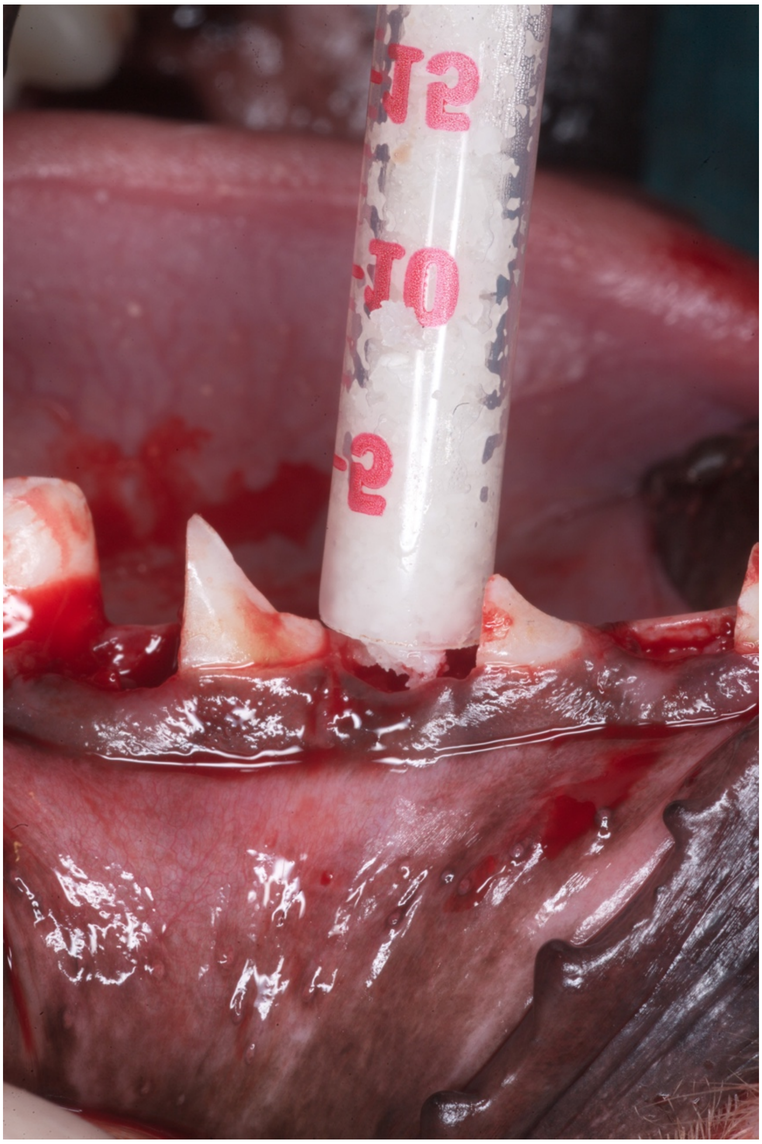


Fig. 4: To close socket orifice and to support surrounding soft tissues, a porcine dermal matrix was applied and sutured over the socket.

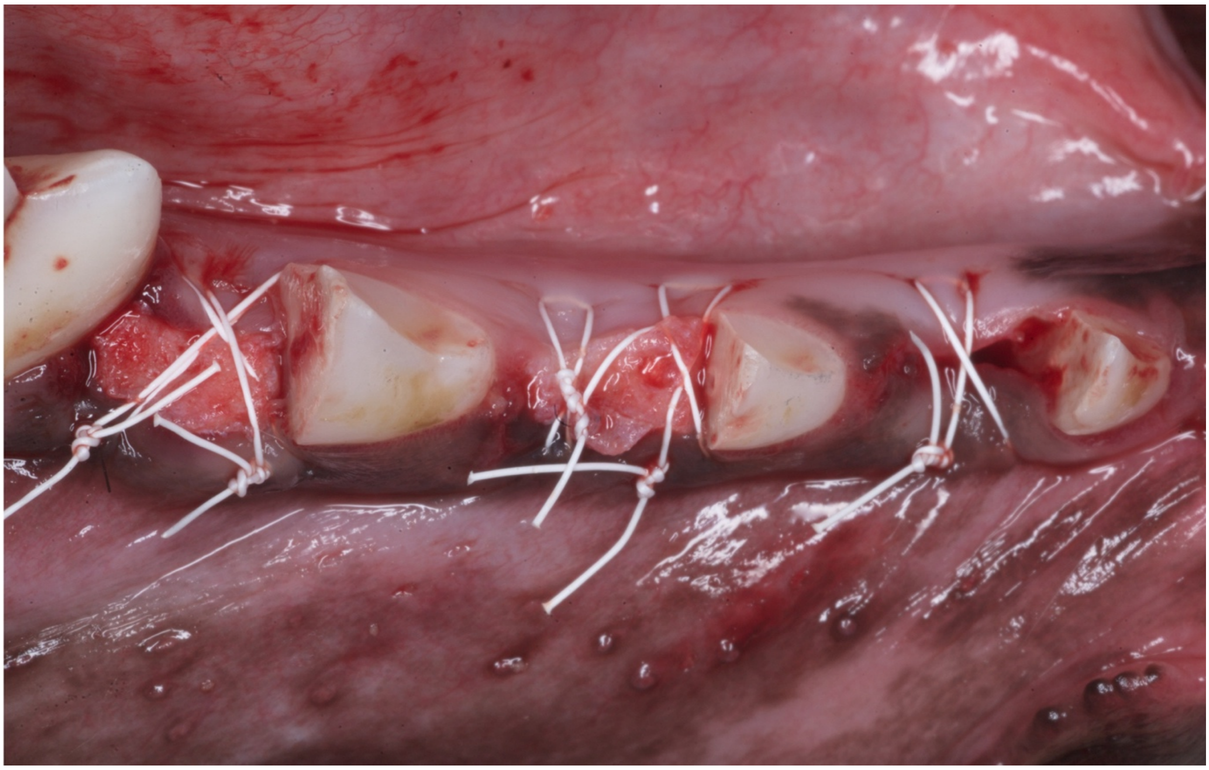
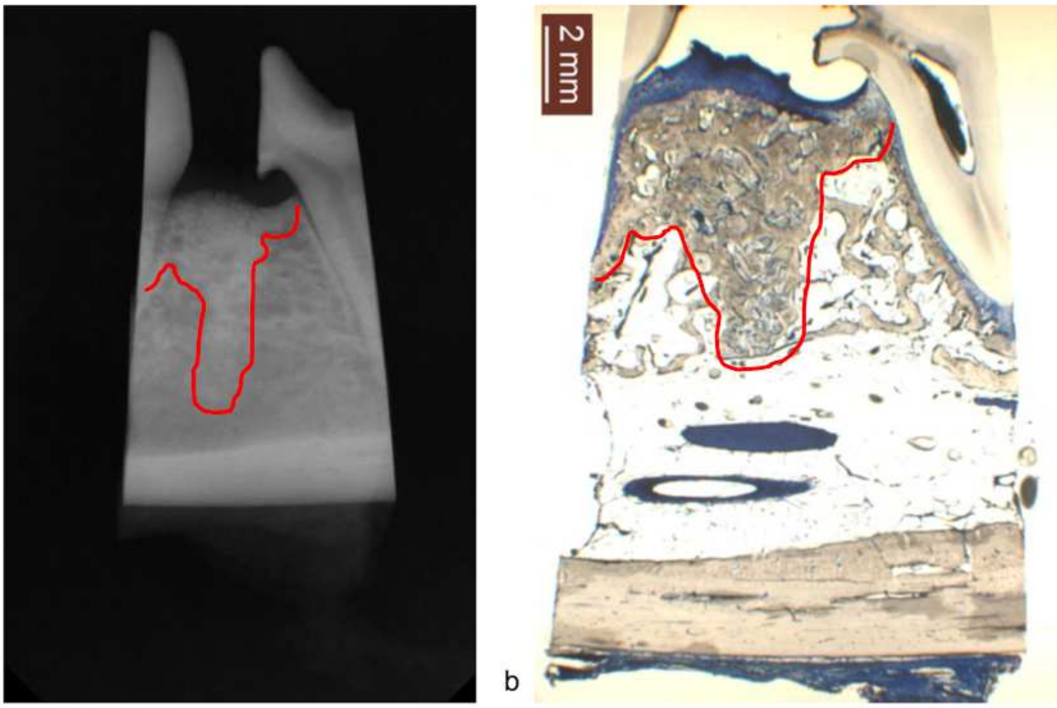


Fig. 5: Augmented socket area between 3rd and 4th mandibular premolars (red line) on a dental film (a) and corresponding area in grinded section (b) (toluidine blue staining, bar = 2mm).



a b

Fig. 6: Serial grinding sections from mesial to distal (from upper row left to lower row right) to demonstrate areas of buccal bone repair (green line) and augmented area (red line) (toluidine blue staining, bar = 2 mm).

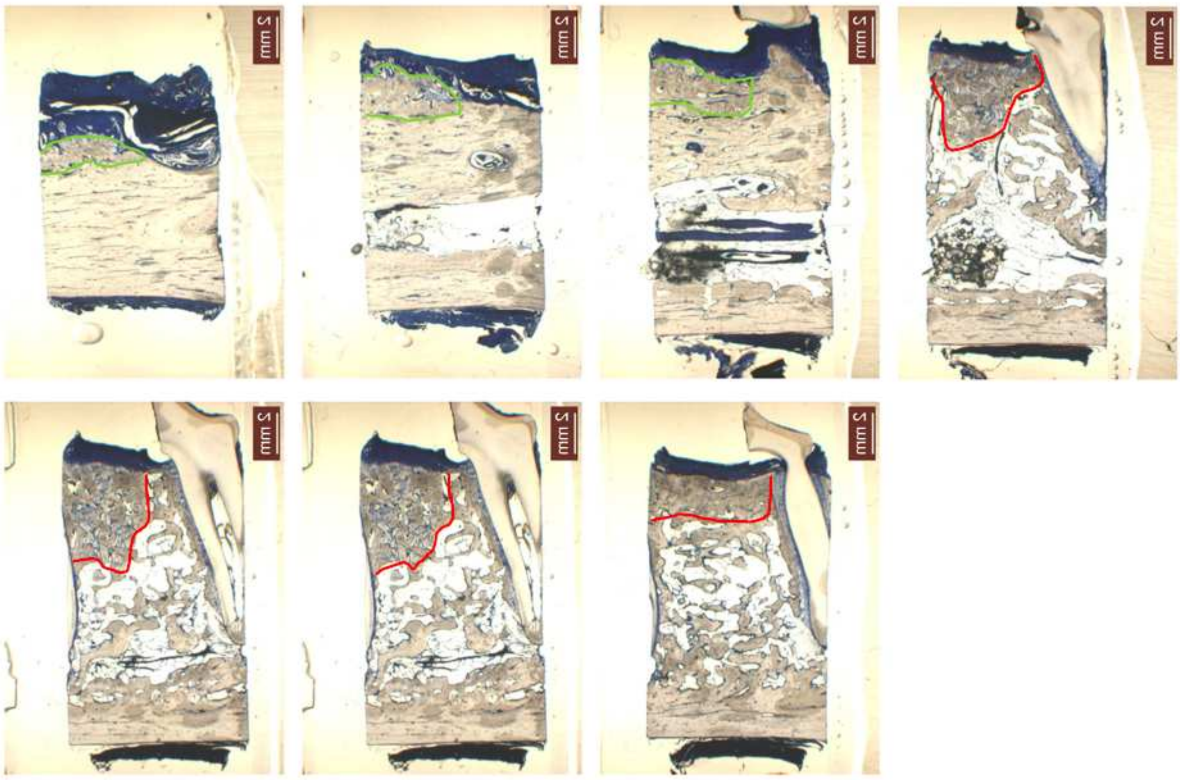


Fig. 7: Histological details from augmented areas: a) Bone substitute granules appearing as cortical bone fragments showing peri-granular osteogenesis (stars); b) newly formed bone bridging two substitute granules (star); c) newly formed bone with ongoing appositional osteogenesis (arrows); d) ongoing resorption of bone substitute granule with resorption lacuna (arrow) with concomitant peri-granular osteogenesis (star) (toluidine blue staining, original magnifications x10 (a), x20 (b, d), x40 (c)).

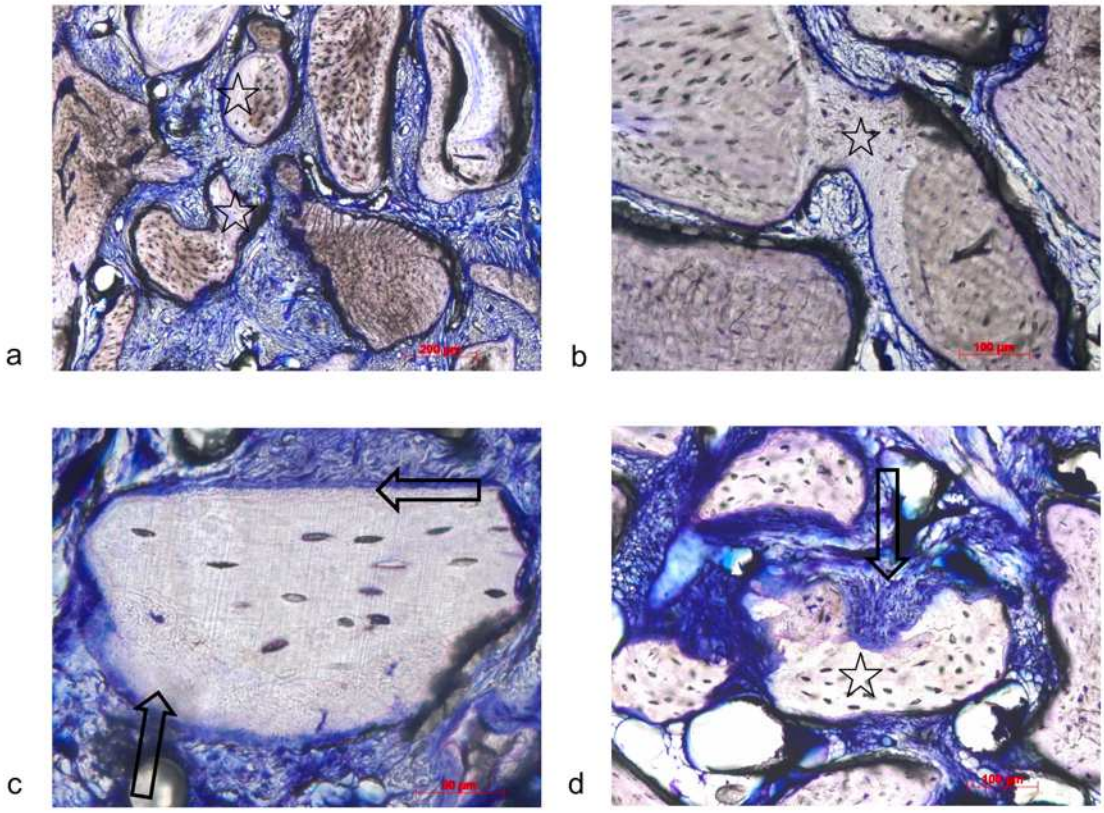
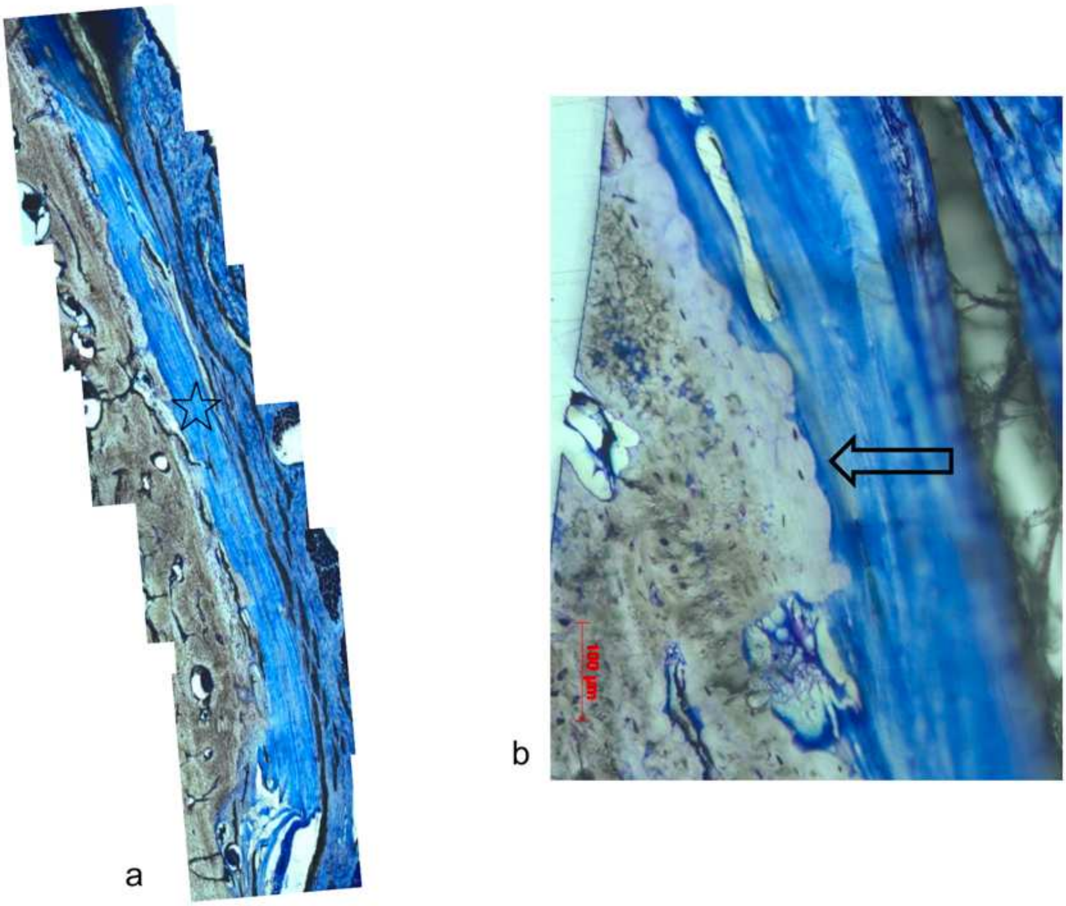


Fig. 8: Histological details from buccal-lingual sections; areas covered by cortical lamina membrane: a) overview: membrane (star) with underlying bone surface (left side) (reconstruction from grinding sections of the same specimen, toluidine staining, original magnification x10); b) higher magnification from a): Bleb-like protrusion indicating appositional osteogenesis at interface to the membrane (arrow) (original magnification x20).



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